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=> file medline hcaplus biosis biotechds embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:20:10 ON 15 MAY 2006

FILE 'HCAPLUS' ENTERED AT 17:20:10 ON 15 MAY 2006
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FILE 'BIOSIS' ENTERED AT 17:20:10 ON 15 MAY 2006
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FILE 'BIOTECHDS' ENTERED AT 17:20:10 ON 15 MAY 2006
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FILE 'EMBASE' ENTERED AT 17:20:10 ON 15 MAY 2006
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=> s binding moiety and anchoring domain and influenza
L1            0 BINDING MOIETY AND ANCHORING DOMAIN AND INFLUENZA

=> s binding domain and anchoring domain and influenza
L2            3 BINDING DOMAIN AND ANCHORING DOMAIN AND INFLUENZA

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3             3 DUP REM L2 (0 DUPLICATES REMOVED)

=> d l3 1-3 ibib ab

L3    ANSWER 1 OF 3  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-17580  BIOTECHDS
TITLE:            New sialidase catalytic domain protein from Actinomyces
                  viscosus, useful for preventing and treating pathogen
                  infection, e.g. viral and bacterial infections, or for
                  treating and reducing allergic and inflammatory responses;
                     sialidase catalytic domain and enhanced recombinant virus
                     vector target cell transduction for gene therapy
AUTHOR:           FANG F; MALAKHOV M
PATENT ASSIGNEE:  FANG F; MALAKHOV M
PATENT INFO:      US 2005112751 26 May 2005
APPLICATION INFO: US 2004-939262 10 Sep 2004
PRIORITY INFO:    US 2004-939262 10 Sep 2004; US 2002-428535 22 Nov 2002
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2005-371672 [38]
AB    DERWENT ABSTRACT:
      NOVELTY - A sialidase catalytic domain protein from Actinomyces viscosus,
      is new.
           DETAILED DESCRIPTION - A sialidase catalytic domain protein
      comprises an amino acid sequence that begins at any of the amino acids
      270-290 of the Actinomyces viscosus sialidase protein sequence comprising
      a fully defined 901 amino acid sequence (SEQ ID NO. 12) given in the
      specification, and ends at any of the amino acids 665-901 of the A.
      viscosus sialidase protein sequence, where the sialidase catalytic domain
      protein lacks the A. viscosus sialidase protein sequence comprising the
      sequence extending from amino acid 1-269, and where the sialidase
      catalytic domain protein has sialidase activity. INDEPENDENT CLAIMS are
      also included for the following: (1) a nucleic acid molecule comprising a
      nucleotide sequence encoding the sialidase catalytic domain protein; (2)
      a fusion protein comprising at least one catalytic domain of a sialidase,
      and a purification domain, a protein tag, a protein stability domain, a
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solubility domain, a protein size-increasing domain, a protein folding domain, a protein localization domain, an **anchoring domain**, an N-terminal domain, a C-terminal domain, a catalytic activity domain, a **binding domain**, or a catalytic activity-enhancing domain; and (3) a pharmaceutical formulation comprising the composition above.

BIOTECHNOLOGY - Preferred Protein: The sialidase catalytic domain protein comprises an amino acid sequence that begins at any of the amino acids 270-290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at any of amino acid residues 665-681. The sialidase catalytic domain protein also comprises a fully defined 394 amino acid sequence (SEQ ID NO. 16) given in the specification. Specifically, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 274 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 666. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Preferred Fusion Protein: The catalytic domain is substantially homologous to the catalytic domain of the Clostridium perfringens sialidase, substantially homologous to the A. viscosus sialidase, substantially homologous to the Arthrobacter ureafaciens sialidase, substantially homologous to the Micromonospora viridifaciens sialidase, substantially homologous to the human Neu2 sialidase, or substantially homologous to the human Neu4 sialidase. Preferably, the catalytic domain is substantially homologous to the catalytic domain of the A. viscosus sialidase. The catalytic domain comprises SEQ ID NO. 16. The fusion protein also comprises at least one **anchoring domain**, where the **anchoring domain** is a GAG-**binding domain**. The **anchoring domain** is substantially homologous to the GAG-**binding domain** of human platelet factor 4 comprising a fully defined 24 amino acid sequence (SEQ ID NO. 2), substantially homologous to the GAG-**binding domain** of human interleukin 8 comprising a fully defined 27 amino acid sequence (SEQ ID NO. 3), substantially homologous to the GAG-**binding domain** of human antithrombin III comprising a fully defined 34 amino acid sequence (SEQ ID NO. 4), substantially homologous to the GAG-**binding domain** of human apoprotein E comprising a fully defined 34 amino acid sequence (SEQ ID NO. 5), substantially homologous to the GAG-**binding domain** of human angio-associated migratory protein comprising a fully defined 12 amino acid sequence (SEQ ID NO. 6), or substantially homologous to the GAG-**binding domain** of human amphiregulin comprising a fully defined 21 amino acid sequence (SEQ ID NO. 7). The **anchoring domain** is substantially homologous to the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). Preferably, it comprises the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). The catalytic domain of a sialidase comprises SEQ ID NO. 16. The fusion protein comprises a fully defined 400 amino acid sequence (SEQ ID NO. 25) given in the specification. The fusion protein further comprises a peptide linker connecting the human amphiregulin GAG-**binding domain** to the catalytic domain of a sialidase. It also comprises fully defined 10-422 amino acid sequences (SEQ ID NO. 27, 29, 31, 33, or 37) given in the specification.

ACTIVITY - Antibacterial; Virucide; Antiallergic; Antiinflammatory; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The sialidase catalytic domain protein is useful for preventing viral infection by **influenza**, parainfluenza, or respiratory syncytial virus by applying an amount of the composition above to epithelial cells of a subject; treating bacterial infections;

and for treating and reducing allergic and inflammatory responses. It can also be used for enhancing transduction of target cells by recombinant viruses.

ADMINISTRATION - Dosage is 1 ng/kg - 10 mg/kg. Administration can be topically, parenterally, intravenously, subcutaneously, intramuscularly, colonically, rectally, nasally, or intraperitoneally.

EXAMPLE - No relevant example given. (82 pages)

L3 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:470946 HCAPLUS
DOCUMENT NUMBER: 141:33763
TITLE: Broad spectrum antivirals comprising a target cell-anchoring GAG-**binding domain** fused with protease inhibitor or sialidase, for treatment and preventing **influenza**
INVENTOR(S): Yu, Mang; Fang, Fang
PATENT ASSIGNEE(S): USA
SOURCE: 75 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004047735	A2	20040610	WO 2003-US37158		20031121
WO 2004047735	A3	20040923			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2506526	AA	20040610	CA 2003-2506526		20031121
EP 1567185	A2	20050831	EP 2003-789884		20031121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CN 1729013	A	20060201	CN 2003-80107241		20031121
JP 2006508193	T2	20060309	JP 2005-510377		20031121
PRIORITY APPLN. INFO.:			US 2002-428535P	P	20021122
			US 2003-464217P	P	20030419
			WO 2003-US37158	W	20031121

AB The present invention provides new protein-based compns. and methods for preventing and treating pathogen infection, particularly **influenza**. The compds. have at least one N-terminal or C-terminal **anchoring domain** that anchors the compd. to the surface of a target epithelial cell, and at least one therapeutic domain that can act extracellularly to prevent infection of the target cell by a pathogen, such as a **influenza** virus. The said **anchoring domain** comprises a GAG-binding motif from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, apolipoprotein E, angio-assocd. cell migratory protein (AAMP), or amphiregulin. The said therapeutic domain comprises enzyme, such as sialidase, or protease inhibitor for host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

L3 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:450844 HCAPLUS
DOCUMENT NUMBER: 143:1221
TITLE: Antiviral proteins blocking infection using

glycosaminoglycan-binding domains to bind protease inhibitors or sialidases to cell surfaces for treatment and preventing **influenza**

INVENTOR(S): Fang, Fang; Malakhov, Michael
PATENT ASSIGNEE(S): USA
SOURCE: 82 pp., Cont.-in-part of U.S. Ser. No. 718,986.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005112751	A1	20050526	US 2004-939262	20040910
US 2005004020	A1	20050106	US 2003-718986	20031121
WO 2006031291	A2	20060323	WO 2005-US25831	20050721

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2002-428535P	P	20021122
US 2003-464217P	P	20030419
US 2003-718986	A2	20031121
US 2004-561749P	P	20040413
US 2004-580084P	P	20040616
US 2004-939262	A	20040910

AB Fusion proteins that use a glycosaminoglycan-**binding domain** to bind antibacterial proteins to a cell surface are described for the treatment of microbial infection, esp. **influenza**. Use of the glycosaminoglycan-binding domains targets the protein to the surface of epithelial cells, and this binds the therapeutic domain to the cell surface to prevent infection of the target cell by a pathogen such as an **influenza** virus. The glycosaminoglycan-binding **anchoring domain** may be from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, or apolipoprotein E. The therapeutic domain may be an enzyme, such as a sialidase, or a protease inhibitor for a host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

```
=> s therapeutic domain and anchoring domain and influenza
L4            3 THERAPEUTIC DOMAIN AND ANCHORING DOMAIN AND INFLUENZA

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5            3 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l5 1-3

L5    ANSWER 1 OF 3  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN    2004-15869  BIOTECHDS
TI    Protein-based compositions comprising a compound having at least one
      therapeutic domain, and one anchoring
      domain, each comprising a peptide or protein, useful for treating
      or preventing pathogen infection, e.g. influenza;
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involving vector-mediated gene transfer and expression in host cell for use in recombinant vaccine preparation
AU YU M; FANG F
PA YU M; FANG F
PI WO 2004047735 10 Jun 2004
AI WO 2003-US37158 21 Nov 2003
PRAI US 2003-464217 19 Apr 2003; US 2002-428535 22 Nov 2002
DT Patent
LA English
OS WPI: 2004-441066 [41]

L5 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:470946 HCAPLUS
DN 141:33763
TI Broad spectrum antivirals comprising a target cell-anchoring GAG-binding domain fused with protease inhibitor or sialidase, for treatment and preventing **influenza**
IN Yu, Mang; Fang, Fang
PA USA
SO 75 pp.
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004047735	A2	20040610	WO 2003-US37158	20031121
	WO 2004047735	A3	20040923		
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	CA 2506526	AA	20040610	CA 2003-2506526	20031121
	EP 1567185	A2	20050831	EP 2003-789884	20031121
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1729013	A	20060201	CN 2003-80107241	20031121
	JP 2006508193	T2	20060309	JP 2005-510377	20031121
PRAI	US 2002-428535P	P	20021122		
	US 2003-464217P	P	20030419		
	WO 2003-US37158	W	20031121		

L5 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:450844 HCAPLUS
DN 143:1221
TI Antiviral proteins blocking infection using glycosaminoglycan-binding domains to bind protease inhibitors or sialidases to cell surfaces for treatment and preventing **influenza**
IN Fang, Fang; Malakhov, Michael
PA USA
SO 82 pp., Cont.-in-part of U.S. Ser. No. 718,986.
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005112751	A1	20050526	US 2004-939262	20040910
	US 2005004020	A1	20050106	US 2003-718986	20031121
	WO 2006031291	A2	20060323	WO 2005-US25831	20050721
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

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NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRAI	US 2002-428535P	P	20021122
	US 2003-464217P	P	20030419
	US 2003-718986	A2	20031121
	US 2004-561749P	P	20040413
	US 2004-580084P	P	20040616
	US 2004-939262	A	20040910

```
=> s therapeutic domain and anchoring domain
L6            3 THERAPEUTIC DOMAIN AND ANCHORING DOMAIN

=> s binding domain and anchoring domain
L7           55 BINDING DOMAIN AND ANCHORING DOMAIN

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8            24 DUP REM L7 (31 DUPLICATES REMOVED)

=> s l8 and infection?
L9            3 L8 AND INFECTION?

=> d l9 1-3 ibib ab

L9   ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:450844  HCAPLUS
DOCUMENT NUMBER:          143:1221
TITLE:                    Antiviral proteins blocking infection using
                          glycosaminoglycan-binding domains to bind protease
                          inhibitors or sialidases to cell surfaces for
                          treatment and preventing influenza
INVENTOR(S):              Fang, Fang; Malakhov, Michael
PATENT ASSIGNEE(S):       USA
SOURCE:                   82 pp., Cont.-in-part of U.S. Ser. No. 718,986.
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005112751	A1	20050526	US 2004-939262	20040910
US 2005004020	A1	20050106	US 2003-718986	20031121
WO 2006031291	A2	20060323	WO 2005-US25831	20050721

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:	US 2002-428535P	P	20021122
	US 2003-464217P	P	20030419
	US 2003-718986	A2	20031121
	US 2004-561749P	P	20040413
	US 2004-580084P	P	20040616
	US 2004-939262	A	20040910

AB Fusion proteins that use a glycosaminoglycan-**binding domain** to bind antibacterial proteins to a cell surface are described for the treatment of microbial **infection**, esp. influenza. Use of the glycosaminoglycan-binding domains targets the protein to the surface of epithelial cells, and this binds the therapeutic domain to the cell surface to prevent **infection** of the target cell by a pathogen such as an influenza virus. The glycosaminoglycan-binding **anchoring domain** may be from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, or apolipoprotein E. The therapeutic domain may be an enzyme, such as a sialidase, or a protease inhibitor for a host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:470946 HCAPLUS
DOCUMENT NUMBER:	141:33763
TITLE:	Broad spectrum antivirals comprising a target cell-anchoring GAG-**binding domain** fused with protease inhibitor or sialidase, for treatment and preventing influenza
INVENTOR(S):	Yu, Mang; Fang, Fang
PATENT ASSIGNEE(S):	USA
SOURCE:	75 pp.
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047735	A2	20040610	WO 2003-US37158	20031121
WO 2004047735	A3	20040923		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506526	AA	20040610	CA 2003-2506526	20031121
EP 1567185	A2	20050831	EP 2003-789884	20031121
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CN 1729013	A	20060201	CN 2003-80107241	20031121
JP 2006508193	T2	20060309	JP 2005-510377	20031121

PRIORITY APPLN. INFO.:	US 2002-428535P	P	20021122
	US 2003-464217P	P	20030419
	WO 2003-US37158	W	20031121

AB The present invention provides new protein-based compns. and methods for preventing and treating pathogen **infection**, particularly influenza. The compds. have at least one N-terminal or C-terminal **anchoring domain** that anchors the compd. to the surface of a target epithelial cell, and at least one therapeutic domain that can

act extracellularly to prevent **infection** of the target cell by a pathogen, such as a influenza virus. The said **anchoring domain** comprises a GAG-binding motif from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, apolipoprotein E, angio-assocd. cell migratory protein (AAMP), or amphiregulin. The said therapeutic domain comprises enzyme, such as sialidase, or protease inhibitor for host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

L9 ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-17580 BIOTECHDS
TITLE: New sialidase catalytic domain protein from Actinomyces viscosus, useful for preventing and treating pathogen **infection**, e.g. viral and bacterial **infections**, or for treating and reducing allergic and inflammatory responses;
sialidase catalytic domain and enhanced recombinant virus vector target cell transduction for gene therapy
AUTHOR: FANG F; MALAKHOV M
PATENT ASSIGNEE: FANG F; MALAKHOV M
PATENT INFO: US 2005112751 26 May 2005
APPLICATION INFO: US 2004-939262 10 Sep 2004
PRIORITY INFO: US 2004-939262 10 Sep 2004; US 2002-428535 22 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-371672 [38]
AB DERWENT ABSTRACT:
NOVELTY - A sialidase catalytic domain protein from Actinomyces viscosus, is new.

DETAILED DESCRIPTION - A sialidase catalytic domain protein comprises an amino acid sequence that begins at any of the amino acids 270-290 of the Actinomyces viscosus sialidase protein sequence comprising a fully defined 901 amino acid sequence (SEQ ID NO. 12) given in the specification, and ends at any of the amino acids 665-901 of the A. viscosus sialidase protein sequence, where the sialidase catalytic domain protein lacks the A. viscosus sialidase protein sequence comprising the sequence extending from amino acid 1-269, and where the sialidase catalytic domain protein has sialidase activity. INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid molecule comprising a nucleotide sequence encoding the sialidase catalytic domain protein; (2) a fusion protein comprising at least one catalytic domain of a sialidase, and a purification domain, a protein tag, a protein stability domain, a solubility domain, a protein size-increasing domain, a protein folding domain, a protein localization domain, an **anchoring domain**, an N-terminal domain, a C-terminal domain, a catalytic activity domain, a **binding domain**, or a catalytic activity-enhancing domain; and (3) a pharmaceutical formulation comprising the composition above.

BIOTECHNOLOGY - Preferred Protein: The sialidase catalytic domain protein comprises an amino acid sequence that begins at any of the amino acids 270-290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at any of amino acid residues 665-681. The sialidase catalytic domain protein also comprises a fully defined 394 amino acid sequence (SEQ ID NO. 16) given in the specification. Specifically, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 274 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 666. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Preferred Fusion Protein: The catalytic domain is substantially homologous to the

catalytic domain of the Clostridium perfringens sialidase, substantially homologous to the A. viscosus sialidase, substantially homologous to the Arthrobacter ureafaciens sialidase, substantially homologous to the Micromonospora viridifaciens sialidase, substantially homologous to the human Neu2 sialidase, or substantially homologous to the human Neu4 sialidase. Preferably, the catalytic domain is substantially homologous to the catalytic domain of the A. viscosus sialidase. The catalytic domain comprises SEQ ID NO. 16. The fusion protein also comprises at least one **anchoring domain**, where the **anchoring domain** is a GAG-**binding domain**. The **anchoring domain** is substantially homologous to the GAG-**binding domain** of human platelet factor 4 comprising a fully defined 24 amino acid sequence (SEQ ID NO. 2), substantially homologous to the GAG-**binding domain** of human interleukin 8 comprising a fully defined 27 amino acid sequence (SEQ ID NO. 3), substantially homologous to the GAG-**binding domain** of human antithrombin III comprising a fully defined 34 amino acid sequence (SEQ ID NO. 4), substantially homologous to the GAG-**binding domain** of human apoprotein E comprising a fully defined 34 amino acid sequence (SEQ ID NO. 5), substantially homologous to the GAG-**binding domain** of human angio-associated migratory protein comprising a fully defined 12 amino acid sequence (SEQ ID NO. 6), or substantially homologous to the GAG-**binding domain** of human amphiregulin comprising a fully defined 21 amino acid sequence (SEQ ID NO. 7). The **anchoring domain** is substantially homologous to the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). Preferably, it comprises the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). The catalytic domain of a sialidase comprises SEQ ID NO. 16. The fusion protein comprises a fully defined 400 amino acid sequence (SEQ ID NO. 25) given in the specification. The fusion protein further comprises a peptide linker connecting the human amphiregulin GAG-**binding domain** to the catalytic domain of a sialidase. It also comprises fully defined 10-422 amino acid sequences (SEQ ID NO. 27, 29, 31, 33, or 37) given in the specification.

ACTIVITY - Antibacterial; Virucide; Antiallergic; Antiinflammatory; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The sialidase catalytic domain protein is useful for preventing viral **infection** by influenza, parainfluenza, or respiratory syncytial virus by applying an amount of the composition above to epithelial cells of a subject; treating bacterial **infections**; and for treating and reducing allergic and inflammatory responses. It can also be used for enhancing transduction of target cells by recombinant viruses.

ADMINISTRATION - Dosage is 1 ng/kg - 10 mg/kg. Administration can be topically, parenterally, intravenously, subcutaneously, intramuscularly, colonically, rectally, nasally, or intraperitoneally.

EXAMPLE - No relevant example given. (82 pages)

```
=> s l8 and pathogen
L10          5 L8 AND PATHOGEN

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11          5 DUP REM L10 (0 DUPLICATES REMOVED)

=> d l11 1-5 ibib ab

L11   ANSWER 1 OF 5  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2005-17580  BIOTECHDS
TITLE:            New sialidase catalytic domain protein from Actinomyces
                  viscosus, useful for preventing and treating pathogen
```

infection, e.g. viral and bacterial infections, or for treating and reducing allergic and inflammatory responses; sialidase catalytic domain and enhanced recombinant virus vector)target cell transduction for gene therapy

AUTHOR: FANG F; MALAKHOV M
PATENT ASSIGNEE: FANG F; MALAKHOV M
PATENT INFO: US 2005112751 26 May 2005
APPLICATION INFO: US 2004-939262 10 Sep 2004
PRIORITY INFO: US 2004-939262 10 Sep 2004; US 2002-428535 22 Nov 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-371672 [38]

AB DERWENT ABSTRACT:

NOVELTY - A sialidase catalytic domain protein from Actinomyces viscosus, is new.

DETAILED DESCRIPTION - A sialidase catalytic domain protein comprises an amino acid sequence that begins at any of the amino acids 270-290 of the Actinomyces viscosus sialidase protein sequence comprising a fully defined 901 amino acid sequence (SEQ ID NO. 12) given in the specification, and ends at any of the amino acids 665-901 of the A. viscosus sialidase protein sequence, where the sialidase catalytic domain protein lacks the A. viscosus sialidase protein sequence comprising the sequence extending from amino acid 1-269, and where the sialidase catalytic domain protein has sialidase activity. INDEPENDENT CLAIMS are also included for the following: (1) a nucleic acid molecule comprising a nucleotide sequence encoding the sialidase catalytic domain protein; (2) a fusion protein comprising at least one catalytic domain of a sialidase, and a purification domain, a protein tag, a protein stability domain, a solubility domain, a protein size-increasing domain, a protein folding domain, a protein localization domain, an **anchoring domain**, an N-terminal domain, a C-terminal domain, a catalytic activity domain, a **binding domain**, or a catalytic activity-enhancing domain; and (3) a pharmaceutical formulation comprising the composition above.

BIOTECHNOLOGY - Preferred Protein: The sialidase catalytic domain protein comprises an amino acid sequence that begins at any of the amino acids 270-290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at any of amino acid residues 665-681. The sialidase catalytic domain protein also comprises a fully defined 394 amino acid sequence (SEQ ID NO. 16) given in the specification. Specifically, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 274 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 666. Alternatively, the sialidase catalytic domain protein comprises an amino acid sequence that begins at amino acid 290 of the A. viscosus sialidase protein sequence (SEQ ID NO. 12) and ends at amino acid residues 681. Preferred Fusion Protein: The catalytic domain is substantially homologous to the catalytic domain of the Clostridium perfringens sialidase, substantially homologous to the A. viscosus sialidase, substantially homologous to the Arthrobacter ureafaciens sialidase, substantially homologous to the Micromonospora viridifaciens sialidase, substantially homologous to the human Neu2 sialidase, or substantially homologous to the human Neu4 sialidase. Preferably, the catalytic domain is substantially homologous to the catalytic domain of the A. viscosus sialidase. The catalytic domain comprises SEQ ID NO. 16. The fusion protein also comprises at least one **anchoring domain**, where the **anchoring domain** is a GAG-**binding domain**. The **anchoring domain** is substantially homologous to the GAG-**binding domain** of human platelet factor 4 comprising a fully defined 24 amino acid sequence (SEQ ID NO. 2), substantially homologous to the GAG-**binding domain** of human interleukin 8 comprising a fully defined 27 amino

acid sequence (SEQ ID NO. 3), substantially homologous to the GAG-**binding domain** of human antithrombin III comprising a fully defined 34 amino acid sequence (SEQ ID NO. 4), substantially homologous to the GAG-**binding domain** of human apoprotein E comprising a fully defined 34 amino acid sequence (SEQ ID NO. 5), substantially homologous to the GAG-**binding domain** of human angio-associated migratory protein comprising a fully defined 12 amino acid sequence (SEQ ID NO. 6), or substantially homologous to the GAG-**binding domain** of human amphiregulin comprising a fully defined 21 amino acid sequence (SEQ ID NO. 7). The **anchoring domain** is substantially homologous to the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). Preferably, it comprises the human amphiregulin GAG-**binding domain** (SEQ ID NO. 7). The catalytic domain of a sialidase comprises SEQ ID NO. 16. The fusion protein comprises a fully defined 400 amino acid sequence (SEQ ID NO. 25) given in the specification. The fusion protein further comprises a peptide linker connecting the human amphiregulin GAG-**binding domain** to the catalytic domain of a sialidase. It also comprises fully defined 10-422 amino acid sequences (SEQ ID NO. 27, 29, 31, 33, or 37) given in the specification.

ACTIVITY - Antibacterial; Virucide; Antiallergic; Antiinflammatory; Respiratory-Gen. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The sialidase catalytic domain protein is useful for preventing viral infection by influenza, parainfluenza, or respiratory syncytial virus by applying an amount of the composition above to epithelial cells of a subject; treating bacterial infections; and for treating and reducing allergic and inflammatory responses. It can also be used for enhancing transduction of target cells by recombinant viruses.

ADMINISTRATION - Dosage is 1 ng/kg - 10 mg/kg. Administration can be topically, parenterally, intravenously, subcutaneously, intramuscularly, colonically, rectally, nasally, or intraperitoneally.

EXAMPLE - No relevant example given. (82 pages)

L11 ANSWER 2 OF 5 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-09746 BIOTECHDS
TITLE: Improving binding of a proteinaceous substance e.g. an AcmA-type protein to a cell-wall material of microorganisms, comprises treating the material with a solution capable of removing protein or carbohydrate from the material; bacterium cell wall material and vector expression in host cell for use in disease diagnosis
AUTHOR: LEENHOUTS C J; RAMASAMY R; STEEN A; KOK J; BUIST G; KUIPERS O P
PATENT ASSIGNEE: APPLIED NANOSYSTEMS BV
PATENT INFO: WO 2002101026 19 Dec 2002
APPLICATION INFO: WO 2002-NL383 11 Jun 2002
PRIORITY INFO: EP 2001-202239 11 Jun 2001; EP 2001-202239 11 Jun 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-167404 [16]
AB DERWENT ABSTRACT:

NOVELTY - Obtaining (M1) cell-wall material of a gram-positive bacterium with improved capacity for binding with a proteinaceous substance (PS), or binding PS to cell-wall material of the bacterium, comprises treating the cell-wall material with a solution capable of removing a cell-wall component such as a protein, (lipo)teichoic acid or carbohydrate from the material.

DETAILED DESCRIPTION - Obtaining (M1) cell-wall material of a gram-positive bacterium with improved capacity for binding with a proteinaceous substance (PS) comprising an AcmA cell wall **binding domain** or its homolog or functional derivative, or binding PS to cell-wall material of the bacterium, comprises treating cell-wall material with a solution capable of removing a cell-wall component such

as a protein, (lipo)teichoic acid or carbohydrate from the material. INDEPENDENT CLAIMS are also included for the following: (1) cell-wall material (I) obtainable by (M1); (2) a pharmaceutical composition comprising (I); (3) a proteinaceous substance (II) comprising a protein anchor of L. lactis (AcmA) cell wall **binding domain** or its homolog or functional derivative, where the domain is a hybrid of two different AcmA cell wall binding domains or their homologs or functional derivatives; (4) a nucleic acid molecule (III) encoding (II); (5) a vector (IV) comprising (III); (6) a micro-organism or expression system comprising (III) or (IV) or capable of expressing (II); and (7) cell wall material provided with (II).

WIDER DISCLOSURE - Also disclosed are chimeric or hybrid AcmA-type anchors.

BIOTECHNOLOGY - Preferred Method: PS further comprises a reactive group such as an antigenic determinant, an enzyme or an antibody, an antibiotic, a hormone, aromatic substance, inorganic particle, or a reporter molecule. The solution comprises an acid preferably acetic acid (HAc), hydrochloric acid (HCl), sulfuric acid (H2SO4), trichloric acid (TCA), trifluoric acid (TFA), or monochloric acid (MCA), more preferably 0.06 - 1.2 M TCA. (M1) comprises heating the cell-wall material in the solution, and pelleting the cell-wall material from the solution. The cell-wall material essentially comprises spherical peptidoglycan microparticles, and is derived from Lactococcus, Lactobacillus, a Bacillus or Mycobacterium spp.. The substance is contacted with the cell wall material at a pH that is lower than the calculated pI value of the AcmA cell wall **binding domain**. Preferred Substance: (II) is provided with a proteinaceous substance comprising an AcmA cell wall **binding domain** or its homolog or functional derivative. (III) comprises a AcmA type domain with relatively high calculated pI, and one with relatively lower calculated pI. One domain is derived from or is functionally equivalent to the AcmA type domain of the lactococcal cell wall hydrolase AcmA or AcmD.

ACTIVITY - Antibacterial; Protozoacide. Protection of mice for lethal Streptococcus pneumoniae challenge after oral immunizations with lactococcal ghosts preloaded with PpmA antigen fused to the lactococcal AcmA protein anchor was investigated. Three l of M17 medium with PpmA::cA obtained after growth and induction for expression of Lactobacillus lactis (pPA32) was centrifuged and filter sterilized to remove all producer cells. Ghost cells were prepared from 0.5 l of L. lactis NZ9000 (DELTAacmA). After binding the ghost cells with PpmA::cA (Ghosts-PpmA::cA) were isolated. Groups of 10 mice were used in the immunizations. Oral doses consisted of 5 x 10 to the power of 9 Ghosts with or without PpmA::CA (50 micrograms) or 50 micrograms soluble PpmA in phosphate buffered saline (PBS). Nasal doses contained 5 x 10 to the power of 8 Ghosts with or without PpmA::cA (5 micrograms) or 5 micrograms soluble PpmA. Subcutaneously, 10 to the power of 8 Ghosts-PpmA::cA (1 micrograms) were injected. The groups of orally immunized mice were intranasally challenged 14 days after the last booster immunization with a dose of 10 to the power of 6 colony forming units (CFU) S. pneumoniae D39. Mice were monitored after the challenge for visible clinical symptoms for 7 days. Serum samples were taken from each mice before the challenge. Ghosts alone either orally or nasally administered (OV Ghosts and IN Ghosts) did not induce anti-PpmA antibodies. Soluble PpmA given by the nasal route resulted in only a low anti-PpmA antibody titer, which was in agreement with the general findings that soluble antigens were not very immunogenic when given by the mucosal routes. Intranasal administration of Ghosts-PpmA::cA resulted in a high titer of anti-PpmA antibodies. Also high titer were obtained by subcutaneous administration of Ghosts-PpmA::cA. Side effects of the orally, nasally or subcutaneously administrated ghosts were not observed. The mice immunized with soluble PpmA or Ghosts alone died within 72 hours post challenge. The group immunized with Ghosts-PpmA::cA showed a survival rate of 40 %. This results showed that mucosal immunization of mice with Ghosts-PpmA was able to induce protective immunity against a lethal S. pneumoniae challenge. In conclusion, the non-recombinant non-living Ghost system

elicited high titer serum antibodies and the mucosal route of administration protected against an mucosally acquired **pathogen**

.

MECHANISM OF ACTION - Vaccine (claimed).

USE - (M1) is useful for improving binding of proteinaceous substance to cell wall material of gram-positive bacterium. A proteinaceous substance (II) comprising a protein anchor of L. lactis (AcmA) cell wall **binding domain** or its homolog or functional derivative, is useful for the preparation of a pharmaceutical composition comprising a vaccine useful for mucosal immunization and for preparing a biocatalyst (claimed). (II) is useful for generating bioadsorbents or biofilters for environmental purposes, microbiocatalysts and diagnostic tools. (II) is useful for vaccination purposes, to elicit immunity for pathogens, like malaria and Streptococcus pneumoniae.

ADMINISTRATION - A vaccine comprising the cell wall is administered mucosally. No dosage is given.

ADVANTAGE - The addition of AcmA-anchor fusion protein results in stable attachment of heterologous proteins to the surface of L. lactis and other gram-positive bacteria. Acid pre-treatment of L. lactis and other gram-positive cells results in high density surface display of heterologous proteins which is a prerequisite for application in industrial processes. The method is highly economically.

EXAMPLE - Lactococcus lactis strain MG1363 or its derivatives like MG1363 DELTAacmA or NZ9000 DELTAacmA were used as recipients for binding of reporter fusion protein, whereas NZ9000 carrying one of the reporter plasmids was used as a production strain. The merozoite surface antigen 2 (MSA2) of Plasmodium falciparum strain 3D7 fused to the three repeats of protein anchor of L.lactis AcmA (cA) (MSA2::cA) was used as the reporter anchor protein. Chemical pretreatment of L. lactis NZ9000AacmA was done with 10 % trichloric acid (TCA). The effect of removal of cell wall components from L. lactis whole cells on binding of the reporter protein MSA2::cA was investigated. L. lactis cells were pretreated with various chemicals or with lysozyme. Pretreatment with TCA, hydrochloric acid (HCl), sulfuric acid (H2SO4) and HAc improved the subsequent binding of MSA2::cA substantially. Other acids that were tested, trifluoric acid (TFA), and monochloric acid (MCA), had similar effects. Minor binding improvements were observed after pretreatment with sodium dodecyl sulfate (SDS), dimethylformamide (DMF), dimethylsulfoxide (DMSO), and dithiothreitol (DTT). Pretreatment of L.lactis cells with the acids TCA, TFA, MCA, HCl, H2SO4 and HAc were the most effective agents to improve binding of cA anchor fusion proteins to lactococcal cells. The binding characteristics of the lactococcal cA homolog cD in a MSA2 fusion was analyzed using the standard TCA pretreatment procedure. A negative control, secreted MSA2 without **anchoring domain** was included in these experiments. In Western blots, the effect of TCA pretreatment on the binding of MSA2::cA was evident. This was also studied using fluorescence microscopy and electron microscopy. Independent of the technique used the effect of TCA pretreatment on the binding of MSA2::cA was clearly detected. The binding of MSA2::cA, MSA2::cD and MSA2 without anchor domain to the Gram-positive bacteria Bacillus subtilis, Lb. casei and M. smegmatis was also analyzed. By Western blot that summarized the binding to non-pretreated and TCA-pretreated B. subtilis cells, a clear increase in binding was observed for MSA2::cA for L. lactis. A MSA2::cA specific signal was also visualized in fluorescence microscopy of non-pretreated B. subtilis cells, but with a highly improved signal for the TCA pretreated cells. Binding of MSA2::cD and MSA2 to non-pretreated or TCA-pretreated cells could not be demonstrated in fluorescence microscopy. Similar results were obtained for Lb. casei cells and M. smegmatis. For MSA2::cD and MSA2 no fluorescence signals were detected. The TCA-pretreatment of M. smegmatis had also a positive effect on the binding of MSA2::cA whereas no binding was observed for MSA2::cD or MSA2. These results indicated that acid pretreatment, such as with TCA, improved the binding of cA protein anchor fusions to the cell surface of Gram-positive bacteria. (77 pages)

L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:278111 HCAPLUS
DOCUMENT NUMBER: 132:305870
TITLE: Fusion proteins containing plant **pathogen** -binding- and toxin domains and transgenic plants with enhanced disease resistance
INVENTOR(S): Fischer, Rainer; Schillberg, Stefan; Nahring, Jorg; Sack, Markus; Monecke, Michael; Liao, Yu-cai; Spiegel, Holger; Zimmerman, Sabine; Emans, Neil; Holzem, Achim
PATENT ASSIGNEE(S): Fraunhofer-Gesellschaft zur Forderung der Angewandten Forschung E.V., Germany
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000023593	A2	20000427	WO 1999-EP7844		19991015
WO 2000023593	A3	20000727			
W: BR, CA, IN, MX					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2345903	AA	20000427	CA 1999-2345903		19991015
BR 9915543	A	20010814	BR 1999-15543		19991015
EP 1123398	A2	20010816	EP 1999-970685		19991015
EP 1123398	B1	20050810			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 301715	E	20050815	AT 1999-970685		19991015
ES 2246093	T3	20060201	ES 1999-970685		19991015
US 6825325	B1	20041130	US 1999-419788		19991018
PRIORITY APPLN. INFO.:			EP 1998-119630	A	19981016
			IN 1998-BO666	A	19981016
			WO 1999-EP7844	W	19991015

AB The invention provides fusion proteins comprising a **pathogen-binding domain** (e.g., an antibody, or part(s) thereof) and a protein which is toxic to the **pathogen** (e.g., an enzyme such as RNase of superoxide dismutase). Also provided are chimeric genes encoding said fusion proteins and their expression in host cells. Expression of the chimeric genes in plants provides transgenic plants with enhanced **pathogen** resistance. These fusion proteins may be expressed and targeted to cellular membranes or plant cell compartments in different orientations and also can be cleaved in vivo by different proteases to become active. These agents are named "mol. pathogenicides". Thus, expression, in tobacco, of a chimeric gene for a anti-tobacco mosaic virus coat protein scFv fused to the transmembrane domain of the human T cell receptor .beta. chain, resulted in enhanced resistance to TMV.

L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:470946 HCAPLUS
DOCUMENT NUMBER: 141:33763
TITLE: Broad spectrum antivirals comprising a target cell-anchoring GAG-**binding domain** fused with protease inhibitor or sialidase, for treatment and preventing influenza
INVENTOR(S): Yu, Mang; Fang, Fang
PATENT ASSIGNEE(S): USA
SOURCE: 75 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004047735	A2	20040610	WO 2003-US37158	20031121
WO 2004047735	A3	20040923		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506526	AA	20040610	CA 2003-2506526	20031121
EP 1567185	A2	20050831	EP 2003-789884	20031121
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1729013	A	20060201	CN 2003-80107241	20031121
JP 2006508193	T2	20060309	JP 2005-510377	20031121
PRIORITY APPLN. INFO.:			US 2002-428535P P	20021122
			US 2003-464217P P	20030419
			WO 2003-US37158 W	20031121

AB The present invention provides new protein-based compns. and methods for preventing and treating **pathogen** infection, particularly influenza. The compds. have at least one N-terminal or C-terminal **anchoring domain** that anchors the compd. to the surface of a target epithelial cell, and at least one therapeutic domain that can act extracellularly to prevent infection of the target cell by a **pathogen**, such as a influenza virus. The said **anchoring domain** comprises a GAG-binding motif from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, apolipoprotein E, angio-assocd. cell migratory protein (AAMP), or amphiregulin. The said therapeutic domain comprises enzyme, such as sialidase, or protease inhibitor for host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:450844 HCAPLUS
DOCUMENT NUMBER: 143:1221
TITLE: Antiviral proteins blocking infection using glycosaminoglycan-binding domains to bind protease inhibitors or sialidases to cell surfaces for treatment and preventing influenza
INVENTOR(S): Fang, Fang; Malakhov, Michael
PATENT ASSIGNEE(S): USA
SOURCE: 82 pp., Cont.-in-part of U.S. Ser. No. 718,986.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005112751	A1	20050526	US 2004-939262	20040910
US 2005004020	A1	20050106	US 2003-718986	20031121
WO 2006031291	A2	20060323	WO 2005-US25831	20050721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,				

SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2002-428535P	P	20021122
US 2003-464217P	P	20030419
US 2003-718986	A2	20031121
US 2004-561749P	P	20040413
US 2004-580084P	P	20040616
US 2004-939262	A	20040910

AB Fusion proteins that use a glycosaminoglycan-**binding domain** to bind antibacterial proteins to a cell surface are described for the treatment of microbial infection, esp. influenza. Use of the glycosaminoglycan-binding domains targets the protein to the surface of epithelial cells, and this binds the therapeutic domain to the cell surface to prevent infection of the target cell by a **pathogen** such as an influenza virus. The glycosaminoglycan-binding **anchoring domain** may be from a mammalian protein, such as human platelet factor 4, interleukin 8, antithrombin III, or apolipoprotein E. The therapeutic domain may be an enzyme, such as a sialidase, or a protease inhibitor for a host enzyme involved in processing a viral protein. Examples of protease inhibitors are aprotinin, leupeptin, soybean proteinase inhibitor, e-aminocaproic acid, or n-p-tosyl-L-lysine.

=> d his

(FILE 'HOME' ENTERED AT 17:19:42 ON 15 MAY 2006)

FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, EMBASE' ENTERED AT 17:20:10 ON 15 MAY 2006

L1	0	S BINDING MOIETY AND ANCHORING DOMAIN AND INFLUENZA
L2	3	S BINDING DOMAIN AND ANCHORING DOMAIN AND INFLUENZA
L3	3	DUP REM L2 (0 DUPLICATES REMOVED)
L4	3	S THERAPEUTIC DOMAIN AND ANCHORING DOMAIN AND INFLUENZA
L5	3	DUP REM L4 (0 DUPLICATES REMOVED)
L6	3	S THERAPEUTIC DOMAIN AND ANCHORING DOMAIN
L7	55	S BINDING DOMAIN AND ANCHORING DOMAIN
L8	24	DUP REM L7 (31 DUPLICATES REMOVED)
L9	3	S L8 AND INFECTION?
L10	5	S L8 AND PATHOGEN
L11	5	DUP REM L10 (0 DUPLICATES REMOVED)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	53.35	53.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.25	-5.25

STN INTERNATIONAL LOGOFF AT 17:28:54 ON 15 MAY 2006

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, May 15, 2006

Hide?	Set Name	Query	Hit Count
		DB=USPT; PLUR=YES; OP=ADJ	
☐	L12	L10 and infection	1904
☐	L11	L10 and inflenza	0
☐	L10	(heparin or heparin sulfate)and (therapeutic domain or protease?)	3516
☐	L9	reporter molecule and anchoring domain	18
☐	L8	binding moiety and anchoring domain	7
☐	L7	binding moiety domain and anchoring domain	0
☐	L6	therapeutic domain and anchoring domain	0
☐	L5	l2 and chimeric protein	1
☐	L4	L2 and therapeutic and anchoring	6
☐	L3	L2 and glycosaminoglycan	1
☐	L2	L1 and treatment	290
☐	L1	influenza infection	314

END OF SEARCH HISTORY

L8: Entry 6 of 7 File: USPT Oct 30, 2001

DOCUMENT-IDENTIFIER: US 6309842 B1
TITLE: Use of modified tethers in screening compound libraries

Detailed Description Text (61):
In some methods, a primary reporter molecule is expressed in a reporter cell and released from the cell where it modifies a secondary reporter in solution outside the cell. For example, the primary reporter molecule can be an enzyme and the secondary reporter molecule, a substrate susceptible to modification by the enzyme. Modification of the substrate can then allow it to bind to a tether. Optionally, the substrate is labelled, or becomes labelled as a result of modification, allowing for separation of modified tethers by virtue of the label. Optionally, the substrate has two domains, one of which allows binding to the tether, the other of which allows detection of the substrate by binding to another moiety, such as antibody. Binding of one or other of the domains to its partner is dependent on modification of the substrate by the reporter.

Detailed Description Text (88):
As noted above, the sensitivity of the assay can sometimes be increased by allowing the reporter molecule to accumulate in cells before the controlled lysis of cells and concomitant release of a burst of reporter molecules. One method of achieving controlled release of a reporter molecule is to link the reporter molecule to a phospholipid anchoring domain and signal secretion sequence as described in commonly owned copending U.S. Ser. No. 08/309,345, filed Sep. 19, 1994 (incorporated by reference in its entirety for all purposes). Usually, the anchoring domain is linked to the C-terminus of the reporter molecule and the signal sequence to the N-terminus of the reporter. The signal sequence directs secretion of the reporter molecule from the cell where it becomes attached to the surface phospholipid layer by the anchoring domain. Controlled release can then be achieved by cleaving the bond between phospholipid and the reporter molecule by addition of a phospholipase to the matrix in which cells and complexes are contacted. For example, the anchoring sequence from the human placental alkaline phosphatase gene CLEPYTACDLAPPAGTTDAAHPGRSVVPALLPLLAGTLLLLETATAP (SEQ ID NO:13) or a subsequence thereof, capable of anchoring the receptor is suitable. Anchored reporter molecules can released from cells by addition of the enzyme phosphoinositol phospholipase C.

Therapeutic domain or Reporter molecule